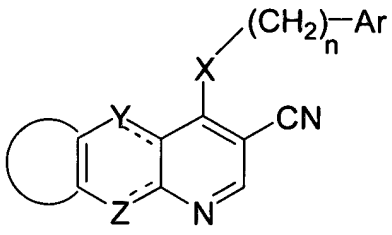
APPENDIX

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

Claim 1 (currently amended). A compound of formula 1 having the structure:



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wherein:

~~Ar is cycloalkyl of 3 to 7 carbon atoms, which may be optionally substituted with one or more alkyl of 1 to 6 carbon atoms; or~~

Ar is a ~~pyridinyl, pyrimidinyl, or~~ phenyl ring; wherein the ~~pyridinyl, pyrimidinyl, or~~ phenyl ring may be optionally mono-, di-, or tri-substituted with substituent(s) independently selected from the group consisting of halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, alkoxycarbonyl of 2-7 carbon atoms, alkanoyl of 2-7 carbon atoms, benzoyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7 carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms, carboxyalkyl of 2-7 carbon atoms, carboalkoxyalkyl of 3-8 carbon atoms, aminoalkyl of 1-5 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-10 carbon atoms, N-alkylaminoalkoxy of 3-9 carbon atoms, N,N-dialkylaminoalkoxy of 4-10 carbon atoms,

mercapto, methylmercapto and benzoylamino; or

~~Ar is a bicyclic aryl or bicyclic heteroaryl ring system of 8 to 12 atoms where the bicyclic heteroaryl ring may contain 1 to 4 heteroatoms selected from N, O, and S wherein the bicyclic aryl or bicyclic heteroaryl ring may be optionally mono- di-, tri, or tetra-substituted with substituent(s) independently selected from the group consisting of halogen, oxo, thiocarbonyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, alkoxycarbonyl of 2-7 carbon atoms, alkanoyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, carboxyalkyl of 2-7 carbon atoms, carboalkoxyalkyl of 3-8 carbon atoms, aminoalkyl of 1-5 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-10 carbon atoms, N-alkylaminoalkoxy of 3-9 carbon atoms, N,N-dialkylaminoalkoxy of 4-10 carbon atoms, mercapto, methylmercapto, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7 carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms, and benzoylamino; or~~

Ar is the radical:

A' is a ~~pyridinyl, pyrimidinyl, or~~ phenyl ring; wherein the ~~pyridinyl, pyrimidinyl, or~~ phenyl ring may be optionally mono- or di-substituted with a substituent(s) independently selected from the group consisting of alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms, halogen, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, alkoxycarbonyl of 2-7 carbon atoms, alkanoyl of 2-7 carbon

atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, carboxyalkyl of 2-7 carbon atoms, carboalkoxyalkyl of 3-8 carbon atoms, aminoalkyl of 1-5 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-10 carbon atoms, N-alkylaminoalkoxy of 3-9 carbon atoms, N,N-dialkylaminoalkoxy of 4-10 carbon atoms, mercapto, methylmercapto, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7 carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms, and benzoylamino;

T is substituted on A' at carbon and is $-NH(CH_2)_m-$, $-O(CH_2)_m-$, $-S(CH_2)_m-$, $-NR(CH_2)_m-$, $-(CH_2)_m-$, $-(CH_2)_mNH-$, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-SO(CH_2)_m-$, $-SO_2(CH_2)_m-$, $-CO(CH_2)_m-$, $-(CH_2)_mCO-$, $-(CH_2)_mSO-$, $-(CH_2)_mSO_2-$ or $-(CH_2)_mNR-$;

L is a phenyl ring that is optionally substituted with one, two, or three substituent(s) independently selected from the group consisting of alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms, halogen, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, alkoxycarbonyl of 2-7 carbon atoms, alkanoyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, carboxyalkyl of 2-7 carbon atoms, carboalkoxyalkyl of 3-8 carbon atoms, aminoalkyl of 1-5 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-10 carbon atoms, N-alkylaminoalkoxy of 3-9 carbon atoms, N,N-dialkylaminoalkoxy of 4-10 carbon atoms, mercapto, methylmercapto, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7 carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms, and benzoylamino; ~~or~~

~~L is a 5- or 6-membered heteroaryl ring where the heteroaryl ring contains 1 to 3 heteroatoms selected from N, O, and S and where the heteroaryl ring may be optionally mono- or di-substituted with substituent(s) selected from the group consisting of halogen, oxo, thiocarbonyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, alkoxycarbonyl of 2-7 carbon atoms, alkanoyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, carboxyalkyl of 2-7 carbon atoms, carboalkoxyalkyl of 3-8 carbon atoms, aminoalkyl of 1-5 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-10 carbon atoms, N-alkylaminoalkoxy of 3-9 carbon atoms, N,N-dialkylaminoalkoxy of 4-10 carbon atoms, mercapto, methylmercapto, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7 carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms, and benzoylamino;~~

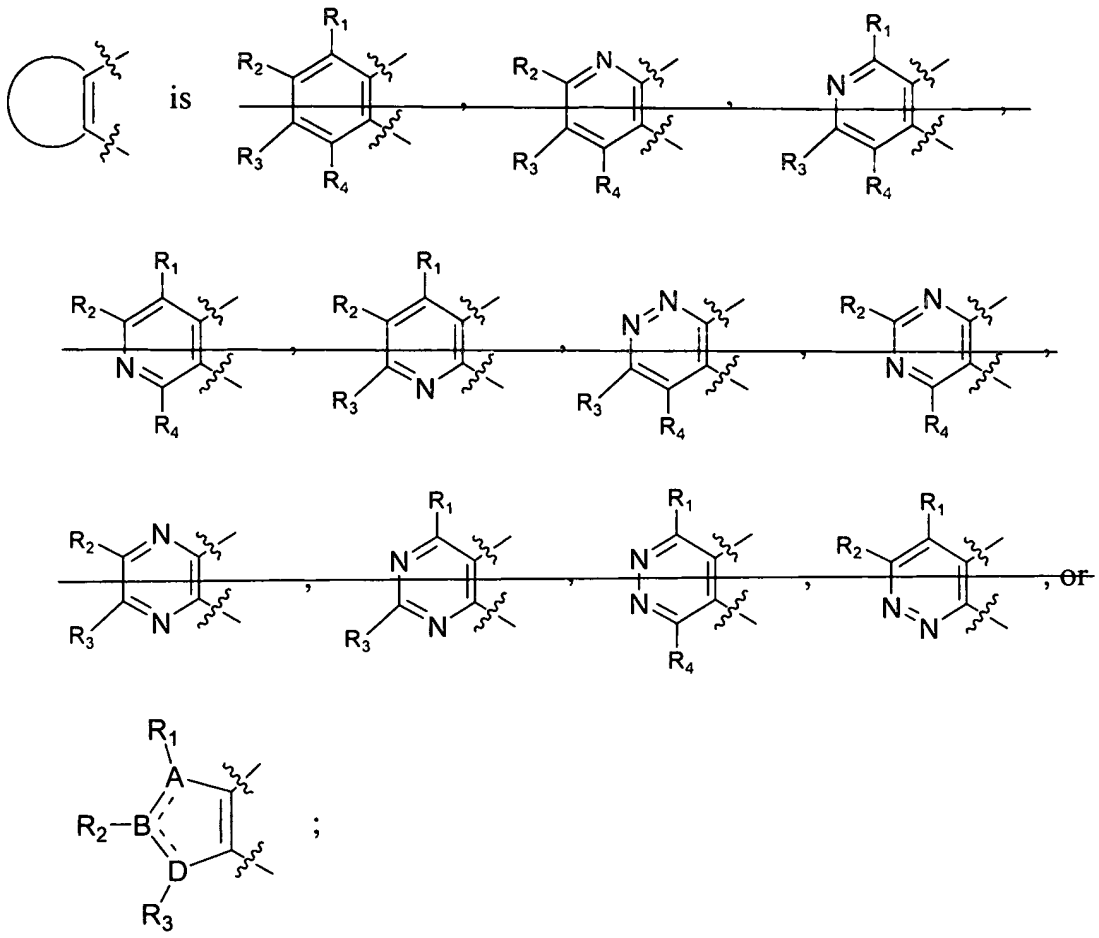
m is 0-3;

n is 0-1;

X is NH~~, O, S,~~ or NR;

R is alkyl of 1-6 carbon atoms;

Y and Z are both carbon ~~or N; the ring structure of formula 1 then being a fused 5,6,6 or 6,6,6 tricycle; or one of Y and Z is N, O or S, and the other is a bond between the two end rings; the ring structure of formula 1 then being a fused 5,5,6 or 6,5,6 tricycle; or one of Y or Z is N with the other being carbon; the ring structure of formula 1 then being a fused 5,6,6 or 6,6,6 tricycle~~;



;

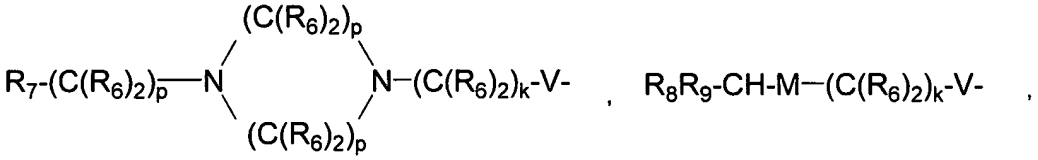
A and D are each~~, independently, carbon,~~ N ~~, O, or S~~;

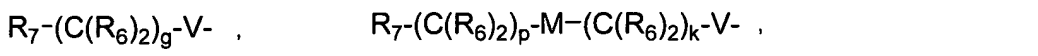
B is carbon~~ or N~~;

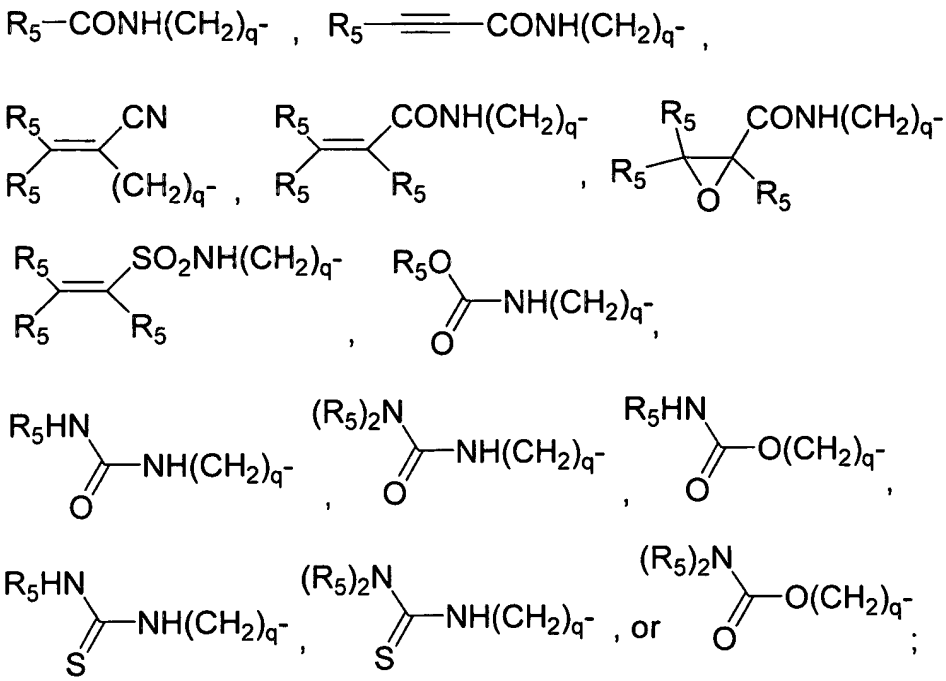
the dashed line indicates an optional double bond;

R_1, R_2, and R_3 ~~, and R_4~~ are each, independently, not present, hydrogen, halogen, hydroxy, amino, hydroxyamino, trifluoromethyl, trifluoromethoxy, mercapto, alkyl of 1-6 carbon atoms, cycloalkyl of 3-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, alkenyloxy of 2-6 carbon atoms, alkynyloxy of 2-6 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, mercaptoalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, cycloalkoxy of 3-8 carbon atoms, alkylthio of 1-6 carbon atoms, cycloalkylthio of 3-8 carbon atoms, alkylsulphinyl of 1-6 carbon atoms, alkylsulfonyl of 1-6 carbon atoms, alkylsulfonamido of 1-6 carbon atoms, alkenylsulfonamido of 2-6 carbon atoms, alkynylsulfonamido of 2-6

carbon atoms, cyano, nitro, carboxy, alkoxycarbonyl of 2-7 carbon atoms, alkanoyl of 2-7 carbon atoms, alkenoyl of 3-7 carbon atoms, N-alkyl-N-alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, phenylamino, benzylamino, phenoxy, phenyl, thiophenoxy, benzyl, alkylamino of 1-6 carbon atoms, alkanoyloxy of 2-7 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7 carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms, dialkylamino of 2 to 12 carbon atoms, alkanoyloxymethyl group of 2-7 carbon atoms, alkenoyloxymethyl group of 2-7 carbon atoms, alkynoyloxymethyl group of 2-7 carbon atoms, azido, benzoyl, carboxyalkyl of 2-7 carbons, carboalkoxyalkyl of 3-8 carbon atoms,







R_5 is independently hydrogen, alkyl of 1-6 carbon atoms, aminoalkyl of 1-6 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-12 carbon atoms, N-cycloalkylaminoalkyl of 4-12 carbon atoms, N-cycloalkyl-N-alkylaminoalkyl of 5-18 carbon atoms, N,N-dicycloalkylaminoalkyl of 7-18 carbon atoms, morpholino-N-alkyl wherein the alkyl group is 1-6 carbon atoms, piperidino-N-alkyl wherein the alkyl group is 1-6 carbon atoms, N-alkyl-piperazino-N-alkyl wherein either alkyl group is 1-6 carbon atoms, azacycloalkyl-N-alkyl of 3-11 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, alkoxyalkyl of 2-8 carbon atoms, or phenyl;

V is $(CH_2)_m$, O, S, or NR_6;

R_7 is NR_6R_6, OR_6, J, $N(R_6)_3^+$, or $NR_6(OR_6)$;

M is NR_6, O, S, N-$[(C(R_6)_2)_pNR_6R_6]$, or N-$[(C(R_6)_2)_p$-$OR_6]$;

W is NR_6, O, S, or is a bond;

Het is a heterocycle selected from the group consisting of morpholine, thiomorpholine, thiomorpholine S-oxide, thiomorpholine S,S-dioxide, piperidine, pyrrolidine, aziridine, pyridine, imidazole, 1,2,3-triazole, 1,2,4-triazole, thiazole, thiazolidine, tetrazole, piperazine, furan, thiophene, tetrahydrothiophene, tetrahydrofuran, dioxane, 1,3-dioxolane pyrrole, and tetrahydropyran; wherein the heterocycle is optionally mono- or

di-substituted on carbon or nitrogen with R_6; optionally mono- or di-substituted on carbon with hydroxy, $-N(R_6)_2$, or $-OR_6$; optionally mono or di-substituted on carbon with the mono-valent radicals $-(C(R_6)_2)_sOR_6$ or $-[(C(R_6)_2)_sN(R_6)_2]$; or optionally mono or di-substituted on a saturated carbon with divalent radicals =O or $-O(C(R_6)_2)_sO-$;

Ph is a phenyl ring optionally mono-, di- or tri-substituted with halogen, alkyl of 1-6 carbon atoms, trifluoromethyl, nitro, cyano, azido, halomethyl, carboxyl, alkoxycarbonyl, alkylthio, mercapto, mercaptomethyl, $-N(R_6)_2$, $-OR_6$, $-(C(R_6)_2)_sOR_6$, $-[(C(R_6)_2)_sN(R_6)_2]$, or $-(C(R_6)_2)_kHet$;

R_6 is hydrogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 1-6 carbon atoms, alkanoyl of 2-7 carbon atoms, carbamoylalkyl of 2-7 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, hydroxycycloalkyl of 3-6 carbon atoms, or carboxyalkyl of 2-7 carbon atoms; or

R_6 is phenyl optionally mono-, di-, or tri-substituted with substituent(s) independently selected from halogen, alkoxy of 1-6 carbon atoms, trifluoromethyl, amino, alkylamino of 1-3 carbon atoms, dialkylamino of 2-6 carbon atoms, nitro, cyano, azido, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, carboxyl, alkoxycarbonyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, phenylamino, benzylamino; alkanoylamino of 1-6 carbon atoms or alkyl of 1-6 carbon atoms;

R_8 and R_9 are each, independently, $-[(C(R_6)_2)_rNR_6R_6]$, and $-[(C(R_6)_2)_r OR_6]$;

J is independently hydrogen, chlorine, fluorine, or bromine;

g = 1-6;

k = 0-4;

p = 2-4;

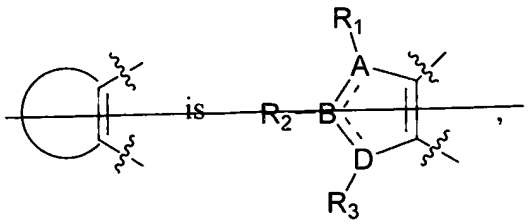
q= 0-4;

r = 1-4;

s = 1-6;

or a pharmaceutically acceptable salt thereof;

provided that ~~when~~



at least one of the bonds between A and B or B and D must be a double bond, with the other being a single bond;

~~at least one of A, B, and D are not carbon;~~

~~only one of A, B, or D can be O or S;~~

~~when A, B, or D is O or S, the adjacent atoms must be carbon;~~

provided that when R_5 is bound to a nitrogen atom, the resulting structures do not include -N-C-N- or -O-C-N- radicals; and when R_5 is bound to an oxygen atom, the resulting structures do not include an -N-C-O- radical;

provided that when R_6 is alkenyl of 2-7 carbon atoms or alkynyl of 2-7 carbon atoms, the alkenyl or alkynyl moieties are bound to a nitrogen or oxygen atom through a saturated carbon atom in the alkenyl or alkynyl chain;

provided that when V is NR_6 and R_7 is NR_6R_6, $N(R_6)_3^+$, or $NR_6(OR_6)$, then g = 2-6;

provided that when M is O or S and R_7 is OR_6, then p = 1-4;

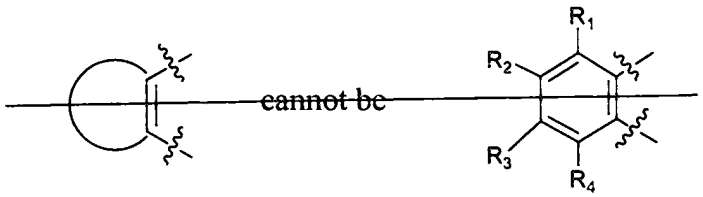
provided that when V is NR_6, O, or S, then k = 2-4;

provided that when V is O or S and M or W is O or S, then k = 1-4;

provided that when W is not a bond with Het bonded through a nitrogen atom then q = 2-4; and

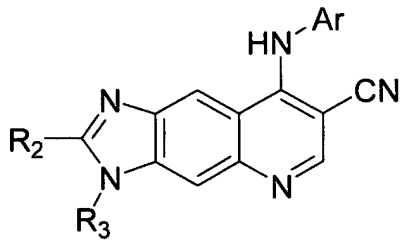
provided that when W is a bond with Het bonded through a nitrogen atom and V is O or NR_6 or S, then k = 2-4; ~~and~~

~~provided that when Ar is a cycloalkyl, a phenyl ring or an optionally substituted phenyl ring, X is NH or NR, and Y and Z are both carbon, then~~



Claims 2-9 (Canceled).

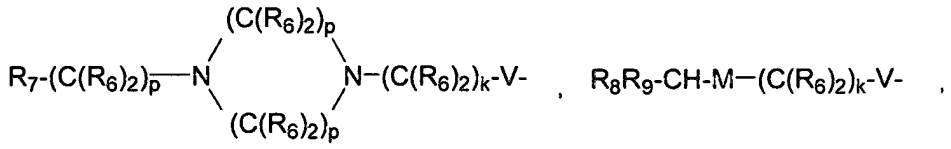
Claim 10 (Original): The compound of claim 1, having the structure

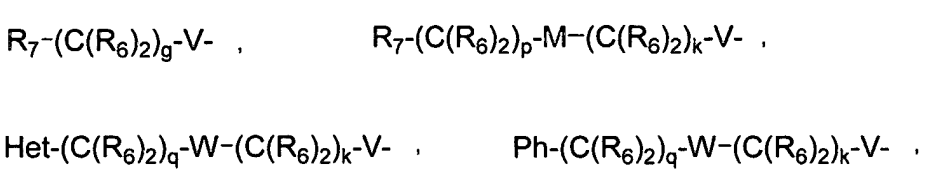


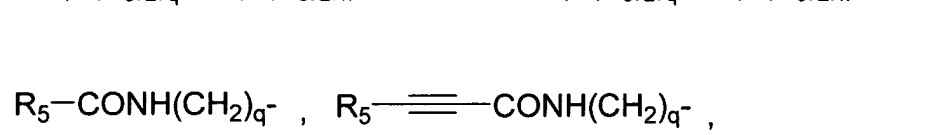
wherein

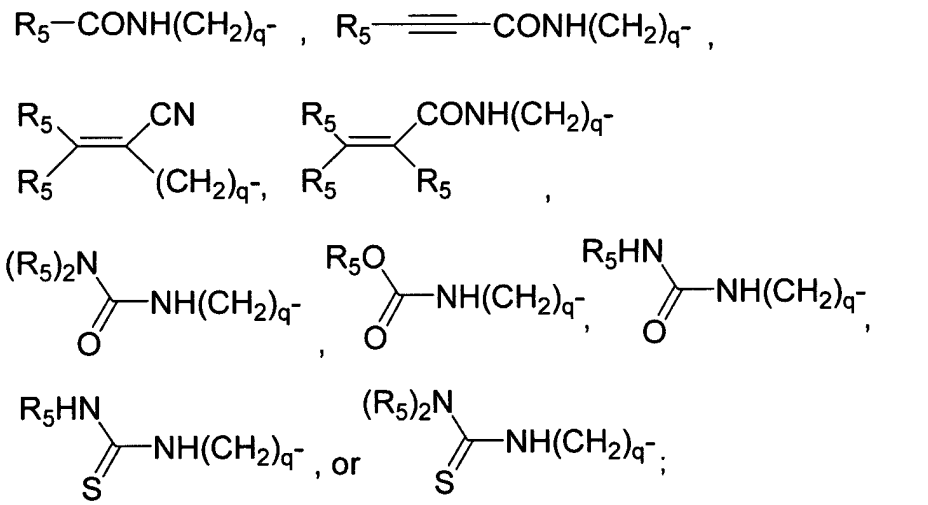
R_2 is hydrogen, amino, hydroxyamino, trifluoromethyl, alkyl of 1-6 carbon atoms, cycloalkyl of 3-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, alkenyloxy of 2-6 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, mercaptoalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, cycloalkoxy of 3-8 carbon atoms, alkylthio of 1-6 carbon atoms, cycloalkylthio of 3-8 carbon atoms, alkylsulphinyl of 1-6 carbon atoms, alkylsulfonyl of 1-6 carbon atoms, alkylsulfonamido of 1-6 carbon atoms, alkenylsulfonamido of 2-6 carbon atoms, alkynylsulfonamido of 2-6 carbon atoms, cyano, carboxy, alkoxycarbonyl of 2-7 carbon atoms, alkanoyl of 2-7 carbon atoms, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7 carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms,N-alkyl-N-alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, phenylamino, benzylamino, phenoxy, phenyl, thiophenoxy, benzyl, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7

carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms,

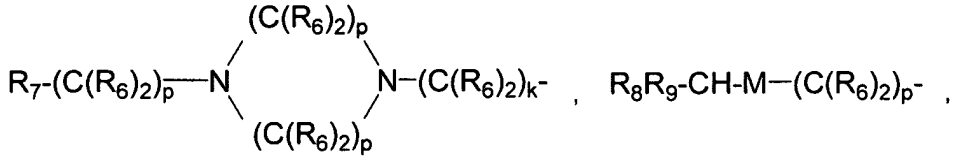








R3 is hydrogen, alkyl of 1-6 carbon atoms, cycloalkyl of 3-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, hydroxyalkyl of 2-6 carbon atoms; mercaptoalkyl of 2-6 carbon atoms, phenyl, benzyl,



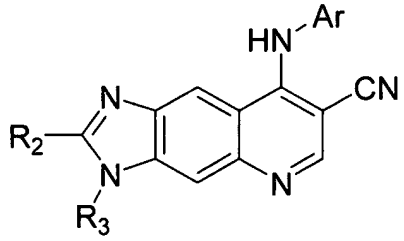
R_7-$(C(R_6)_2)_p$- , R_7-$(C(R_6)_2)_p$-M-$(C(R_6)_2)_p$- ,

Het-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_p$- , Ph-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_p$- ,

or a pharmaceutically acceptable salt thereof.

Claims 11-18 (Canceled).

Claim 19 (Original): The compound of claim 1, having the structure



wherein

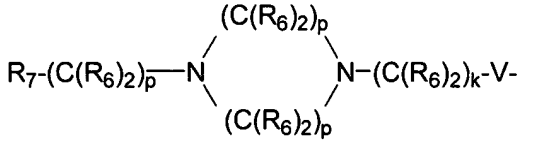
Ar is a phenyl ring which may be optionally mono-, di- or tri-substituted with a substituent selected from the group consisting of halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, alkoxycarbonyl of 2-7 carbon atoms, alkanoyl of 2-7 carbon atoms, benzoyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2-12 carbon atoms, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7 carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms, and benzoylamino; or

Ar is the radical:

;

R_2 is hydrogen, amino, hydroxyamino, trifluoromethyl, alkyl of 1-6 carbon atoms, cycloalkyl of 3-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, alkenyloxy

of 2-6 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, mercaptoalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, cycloalkoxy of 3-8 carbon atoms, alkylthio of 1-6 carbon atoms, cycloalkylthio of 3-8 carbon atoms, alkylsulphinyl of 1-6 carbon atoms, alkylsulfonyl of 1-6 carbon atoms, alkylsulfonamido of 1-6 carbon atoms, alkenylsulfonamido of 2-6 carbon atoms, alkynylsulfonamido of 2-6 carbon atoms, cyano, carboxy, alkoxycarbonyl of 2-7 carbon atoms, alkanoyl of 2-7 carbon atoms, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7 carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms,N-alkyl-N-alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, phenylamino, benzylamino, phenoxy, phenyl, thiophenoxy, benzyl, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, carbamoyl, N-alkylcarbamoyl of 2-7 carbon atoms, N,N-dialkylcarbamoyl of 3-13 carbon atoms,

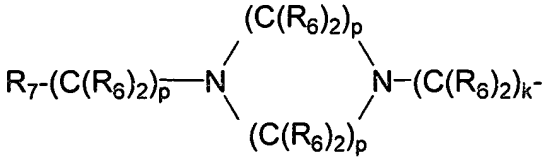


, R_8R_9-CH-M—$(C(R_6)_2)_k$-V- ,

R_7-$(C(R_6)_2)_g$-V- , R_7-$(C(R_6)_2)_p$-M—$(C(R_6)_2)_k$-V- ,

Het-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_k$-V- , Ph-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_k$-V- ,

R3 is hydrogen, alkyl of 1-6 carbon atoms, cycloalkyl of 3-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, hydroxyalkyl of 2-6 carbon atoms; mercaptoalkyl of 2-6 carbon atoms, phenyl, benzyl,



, R_8R_9-CH-M—$(C(R_6)_2)_p$- ,

R_7-$(C(R_6)_2)_p$- , R_7-$(C(R_6)_2)_p$-M-$(C(R_6)_2)_p$- ,

Het-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_p$- , Ph-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_p$- ,

or a pharmaceutically acceptable salt thereof.

Claim 20 (Currently amended): The compound of claim 1, which is:

~~a) 8-(3,4,5-trimethoxyanilino)-3H-[1,2,3]triazolo[4,5-g]quinoline-7-carbonitrile,~~

~~b) 9-(4-chloro-5-methoxy-2-methylanilino)pyrido[2,3-g]quinoxaline-8-carbonitrile,~~

~~c)~~ a) 8-(5-methoxy-2-methylanilino)-2-{[2-(4-morpholinyl)ethyl]amino}imidazo[4,5-g]quinoline-7-carbonitrile,

~~d)~~ b) 2-{[2-(4-morpholinyl)ethyl]amino}-8-(3,4,5-trimethoxyanilino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~e)~~ c) 2-amino-8-(4-phenoxyanilino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~f)~~ d) 8-(3-bromo-phenylamino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~g)~~ e) 8-(2-bromo-4-chlorophenylamino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~h)~~ f) 8-(2-bromo-4-chloro-5-methoxyphenylamino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~i)~~ g) 8-(2-chloro-5-methoxyphenylamino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~j)~~ h) 8-(3-hydroxy-4-methylphenylamino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~k)~~ i) 8-(3,4,5-trimethoxyanilino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~l)~~ j) 8-(4-phenoxyanilino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~m)~~ k) 2-(chloromethyl)-8-(3,4,5-trimethoxyanilino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~n)~~ l) 2-(4-morpholinylmethyl)-8-(3,4,5-trimethoxyanilino)imidazo[4,5-g]quinoline-7-carbonitrile,

~~o)~~ m) 8-(4-chloro-5-methoxy-2-methylanilino)-3-[2-(4-morpholinyl)ethyl]-3H-imidazo[4,5-g]quinoline-7-carbonitrile,

~~p)~~ ~~n)~~ 3-[2-(4-morpholinyl)ethyl]-8-(4-phenoxyanilino)-3H-imidazo[4,5-g]quinoline-7-carbonitrile,

~~q) 8-[(4-chloro-5-methoxy-2-methylphenyl)amino]-thiazolo[4,5-g]quinoline-7-carbonitrile;~~

~~r) 4-(3-bromophenylamino)benzo[4,5]thieno[3,2-b]pyridine-3-carbonitrile;~~

~~s) 4-(4-chloro-2-fluorophenylamino)benzo[4,5]thieno[3,2-b]pyridine-3-carbonitrile;~~

~~t) 4-(2,4-dichlorophenylamino)benzo[4,5]thieno[3,2-b]pyridine-3-carbonitrile;~~

~~u) 4-(2,4-dichloro-5-methoxyphenylamino)benzo[4,5]thieno[3,2-b]pyridine-3-carbonitrile;~~

~~v) 4-(4-phenoxyphenylamino)benzo[4,5]thieno[3,2-b]pyridine-3-carbonitrile;~~

~~w) 4-(3-hydroxy-4-methylphenylamino)benzo[4,5]thieno[3,2-b]pyridine-3-carbonitrile;~~

~~x) 4-(4-chloro-2-fluorophenoxy)benzo[4,5]thieno[3,2-b]pyridine-3-carbonitrile;~~

~~y) 4-(4-chloro-5-methoxy-2-methylphenylamino)-8-nitrobenzo[4,5]thieno[3,2-b]pyridine-3-carbonitrile;~~

~~z) 8-amino-4-(4-chloro-5-methoxy-2-methylanilino)[1]benzothieno[3,2-b]pyridine-3-carbonitrile;~~

~~aa) 4-(3-bromoanilino)-6-nitro[1]benzothieno[3,2-b]pyridine-3-carbonitrile;~~

~~bb) 6-amino-4-(3-bromoanilino)[1]benzothieno[3,2-b]pyridine-3-carbonitrile;~~

~~cc) 4-(3-bromophenylamino)benzo[4,5]furo[3,2-b]pyridine-3-carbonitrile;~~

~~dd) 4-(4-chloro-2-fluorophenylamino)benzo[4,5]furo[3,2-b]pyridine-3-carbonitrile;~~

~~ee) 4-(3-hydroxy-4-methylphenylamino)benzo[4,5]furo[3,2-b]pyridine-3-carbonitrile;~~

~~ff) 4-(4-phenoxyphenylamino)benzo[4,5]furo[3,2-b]pyridine-3-carbonitrile;~~

~~gg) 4-(4-chloro-2-fluorophenoxy)benzo[4,5]furo[3,2-b]pyridine-3-carbonitrile;~~

~~hh) 4-(2,4-dichloroanilino)-8-nitro[1]benzothieno[3,2-b]pyridine-3-carbonitrile;~~

~~ii) 4-(3-bromoanilino)-8-nitro[1]benzothieno[3,2-b]pyridine-3-carbonitrile;~~

~~jj) 8-amino-4-(3-bromoanilino)[1]benzothieno[3,2-b]pyridine-3-carbonitrile;~~

~~kk) N-[4-(3-bromoanilino)-3-cyano[1]benzothieno[3,2-b]pyridin-8-yl]acrylamide;~~

~~ll) N-[4-(3-bromoanilino)-3-cyano[1]benzothieno[3,2-b]pyridin-6-yl]acrylamide;~~

~~mm) 4-(2,4-Dichloro-5-methoxyanilino)-7,8-dimethoxybenzo[b] [1,8]naphthyridine-3-~~

~~carbonitrile;~~

~~nn) 8-(2-Chloroethoxy)-4-(2,4-dichloro-5-methoxyanilino)-7-methoxybenzo[b][1,8]naphthyridine-3-carbonitrile;~~

~~oo) 4-(2,4-Dichloro-5-methoxyanilino)-7-methoxy-8-[2-(4-morpholinyl)ethoxy]benzo[b][1,8]naphthyridine-3-carbonitrile;~~

~~pp) 8-(2-Chloroethoxy)-4-{3-chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-methoxybenzo[b][1,8]naphthyridine-3-carbonitrile;~~

~~qq) 4-(2,4-Dichloro-5-methoxyanilino)-7-methoxy-8-[2-(4-methyl-1-piperazinyl)ethoxy]benzo[b][1,8]naphthyridine-3-carbonitrile;~~

~~rr) 4-{3-Chloro-4-[(1-methyl-1H-imidazol-2-yl)sulfanyl]anilino}-7-methoxy-8-[2-(4-morpholinyl)ethoxy]benzo[b][1,8]naphthyridine-3-carbonitrile;~~

~~ss) 4-(2,4-Dichloroanilino)-7,8-dimethoxybenzo[b][1,8]naphthyridine-3-carbonitrile~~

or a pharmaceutically acceptable salt thereof.

Claim 21 (Canceled).

Claim 22 (Original): A method of treating, inhibiting the growth of, or eradicating a neoplasm in a mammal in need thereof which comprises providing to said mammal an effective amount of a compound as described in claim 1.

Claim 23 (Original): The method according to claim 22 wherein the neoplasm is selected from the group consisting of breast, kidney, bladder, mouth, larynx, esophagus, stomach, colon, ovary, lung, pancreas, liver, prostate, and skin.

Claim 24 (Original): The method according to claim 22 wherein the neoplasm expresses EGFR or erbB2 (Her2).

Claim 25 (Original): The method according to claim 22 wherein the neoplasm depends, at least in part, on the MAPK pathway.

Claim 26 (Currently amended): The method ~~acording~~ according to claim 22 wherein the neoplasm depends, at least in part, on the RAF kinase pathway.

Claim 27 (Currently amended): The method ~~acording~~ according to claim 22 wherein the neoplasm depends, at least in part, on the SRC kinase pathway.

Claim 28 (Currently amended): The method according to claim 22 wherein the neoplasm depends, at least in part, on the ~~ECK/LERK-1~~ Mek-Erk pathway.

Claim 29 (Original): The method according to claim 22 wherein the neoplasm depends, at least in part, on the VEGF/KDR pathway.

Claim 30 (Original): A method of treating, inhibiting the progression of, or eradicating polycystic kidney disease in a mammal in need thereof which comprises providing to said mammal an effective amount of a compound described in claim 1.

Claim 31 (Original): A method of treating, inhibiting, or eradicating colonic polyps in a mammal in need thereof which comprises providing to said mammal an effective amount of a compound described in claim 1.

Claim 32 (Original): A method of inhibiting the biological effects of a deregulated protein kinase in a mammal which comprises providing to said mammal an effective amount of a compound described in claim 1.

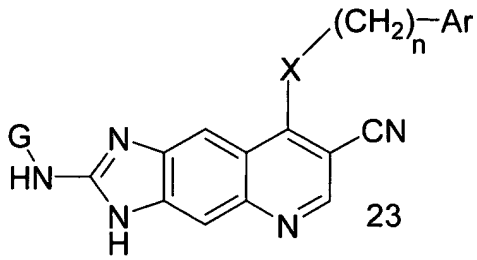
Claim 33 (Original): A method of treating a disease or inhibiting a disease state whose etiology is at least in part caused by a defect in a signaling pathway upstream from a protein kinase; by overexpression of a protein kinase; or by a dysregulated protein kinase in a mammal in need thereof which comprises providing to said mammal an effective amount of a compound described in claim 1.

Claim 34 (Original): A pharmaceutical composition which comprises a pharmaceutically acceptable carrier and a compound described in claim 1.

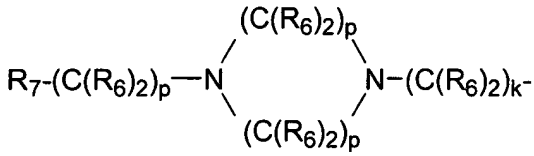
Claim 35 (Canceled).

Claim 36 (New): A process for the preparation of a compound described in claim 1 which comprises one or more of the following steps:

A) preparing a substituted 2-amino-7-cyanoimidazo[4,5-g]quinoline of formula 23



wherein Ar, X and n are as defined in claim 1 and G is selected from the group consisting of alkyl of 1-6 carbon atoms, cycloalkyl of 3-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, hydroxyalkyl of 2-6 carbon atoms, mercaptoalkyl of 2-6 carbon atoms, phenyl, benzyl,



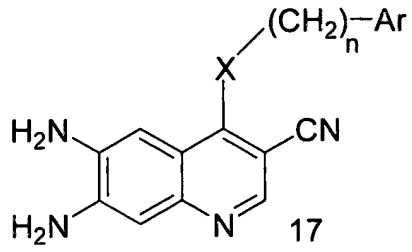
, R_8R_9-CH-M–$(C(R_6)_2)_k$- ,

R_7-$(C(R_6)_2)_p$- , R_7-$(C(R_6)_2)_p$-M–$(C(R_6)_2)_p$- ,

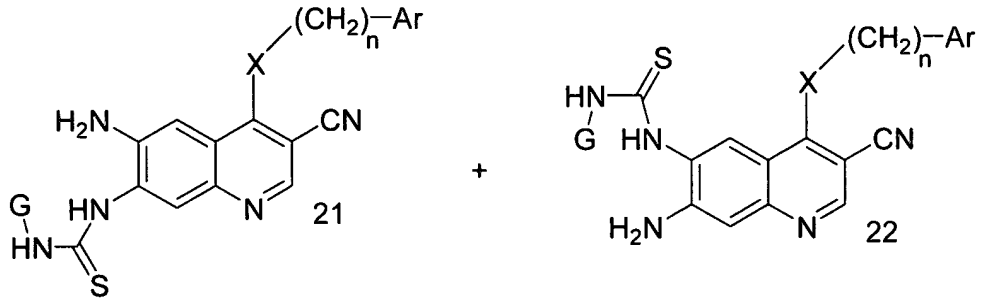
Het-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_p$- and Ph-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_p$- ,

wherein R_6, R_7, R_8, R_9, M, W, Het, Ph, p and q are as defined in claim 1, g = 2-6 and k = 2-4;

which comprises reacting a compound of formula 17



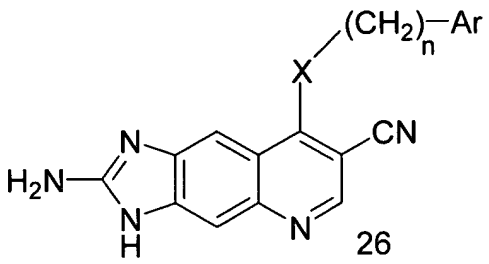
with an isothiocyanate GN=C=S in an inert solvent to produce a mixture of thiourea compounds of formulas 21 and 22



wherein Ar, X, G and n are as defined hereinabove;

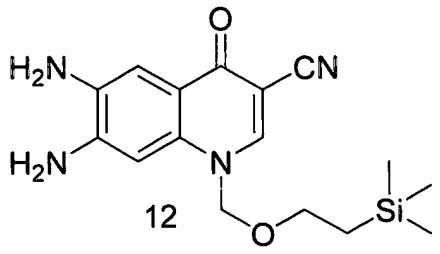
heating said mixture of thiourea compounds of formulas 21 and 22 with mercury (II) oxide and a catalytic amount of sulfur in an inert solvent to provide the corresponding substituted 2-amino-7-cyanoimidazo[4,5-g]quinoline of formula 23;

B) preparing a 7-cyano imidazo[4,5-g]quinoline of formula 26



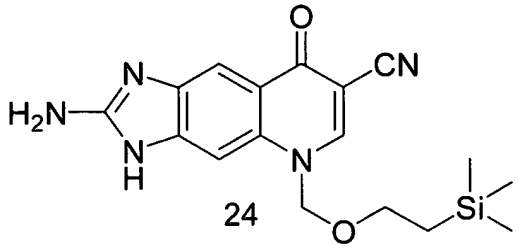
wherein Ar, X and n are as defined in claim 1;

which comprises reacting a compound of formula 12



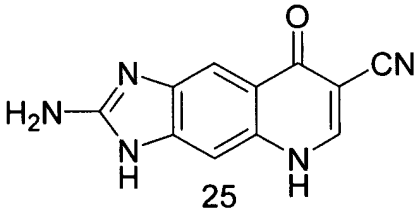
12

with cyanogen bromide in an inert solvent to provide a compound of formula 24



24

refluxing the compound of formula 24 in formic acid with four equivalents of imidazole to provide a compound of formula 25



25

heating the compound of formula 25 with a chlorinating agent in the presence or absence of a solvent to provide the corresponding 2-amino-8-chloroimidazo[4,5-g]quinoline-7-carbonitrile;

condensing the corresponding 2-amino-8-chloroimidazo[4,5-g]quinoline-7-carbonitrile with a nucleophilic amine, aniline, mercaptan, thiophenol, phenol or alcohol reagent of formula 5

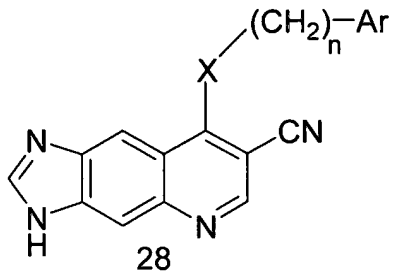
$$HX-(CH_2)_n-Ar$$

5

wherein Ar, X and n are as defined hereinabove; and optionally accelerating the condensation step by heating the reaction mixture together with one equivalent of

pyridine hydrochloride or by using a base selected from the group consisting of trialkylamine, sodium hydride in an inert solvent, sodium alkoxide in an alcohol solvent and potassium alkoxide in an alcohol solvent, to give the 7-cyano imidazo[4,5-g]quinolines of formula 26;

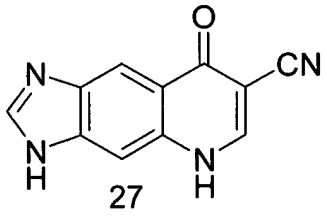
C) preparing a 7-cyano imidazo[4,5-g]quinoline of formula 28



28

wherein Ar, X and n are as defined in claim 1;

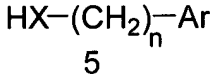
which comprises refluxing the compound of formula 12 described hereinabove in Step B in formic acid with four equivalents of imidazole to provide a compound of formula 27



27

heating the compound of formula 27 with a chlorinating agent in the presence or absence of a solvent to provide the corresponding 8-chloroimidazo[4,5-g]quinoline-7-carbonitrile;

condensing the corresponding 8-chloroimidazo[4,5-g]quinoline-7-carbonitrile with a nucleophilic amine, aniline, mercaptan, thiophenol, phenol, or alcohol reagent of formula 5



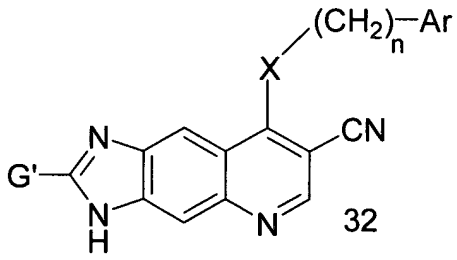
5

wherein Ar, X and n are as defined hereinabove; and optionally accelerating the condensation step by heating the reaction mixture together with one equivalent of

pyridine hydrochloride or by using a base selected from the group consisting of trialkylamine, sodium hydride in an inert solvent, sodium alkoxide in an alcohol solvent and potassium alkoxide in an alcohol solvent, to give the 7-cyano-imidazo[4,5-g]quinoline of formula 28; or,

alternatively preparing the above 7-cyanoimidazo[4,5-g]quinoline compound of formula 28 described hereinabove by refluxing the compound of formula 17 described hereinabove in Step A in diethoxymethyl acetate to provide the corresponding 7-cyanoimidazo[4,5-g]quinolin-8-ylformamide; and heating the 7-cyanoimidazo[4,5-g]quinolin-8-ylformamide with potassium carbonate in methanol or ethanol to provide the 7-cyano-imidazo[4,5-g]quinoline compound of formula 28;

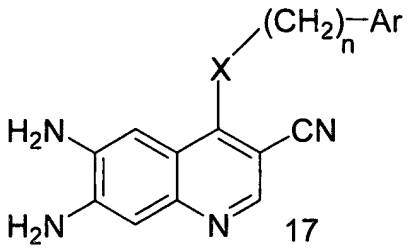
D) preparing a 7-cyano-imidazo[4,5-g]quinoline of formula 32



32

wherein Ar, X and n are as defined in claim 1 and G' is selected from the group consisting of hydrogen, alkyl of 1-6 carbon atoms, trifluoromethyl, cycloalkyl of 3-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, thiol, hydroxyalkyl of 1-6 carbon atoms, mercaptoalkyl of 1-6 carbon atoms, halomethyl, alkoxycarbonyl of 2-7 carbon atoms, phenyl, benzyl, phenoxy, R_7-$(C(R_6)_2)_g$-V- and Ph-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_k$-V-, wherein g, k, q, R_6, R_7, V, W and Ph are as defined hereinabove;

which comprises reacting a compound of formula 17

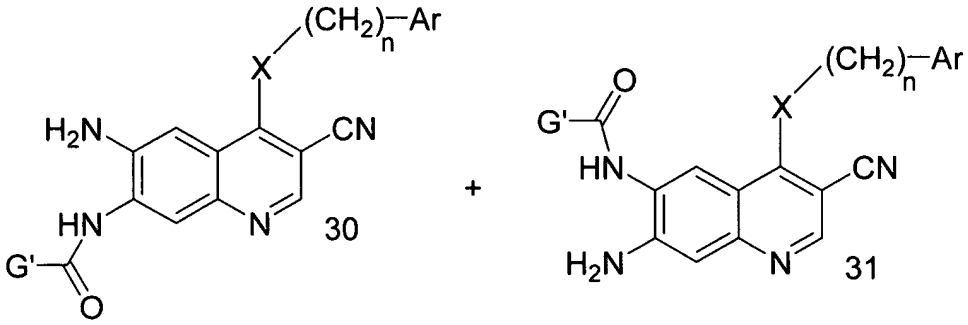


wherein Ar, X and n are as defined in claim 1;

with a carboxylic acid chloride of formula 29

G'COCL

with a base selected from the group consisting of pyridine, diethylaniline and triethylamine with or without an inert solvent to provide a mixture of compounds of formulas 30 and 31



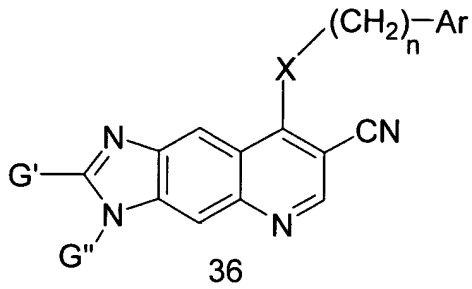
wherein Ar, X and n are as defined in claim 1 and G' is as defined hereinabove;

heating the mixture of the compounds of formulas 30 and 31 in formic acid or acetic acid to provide the corresponding substituted 7-cyano-imidazo[4,5-g]quinolines of formula 32; and, optionally, converting the G' group of formula 32 to an R_2 group of formula 1 as defined in claim 1; or,

alternatively preparing the above 7-cyano-imidazo[4,5-g]quinoline of formula 32 described hereinabove by reacting the above compound of formula 17 described

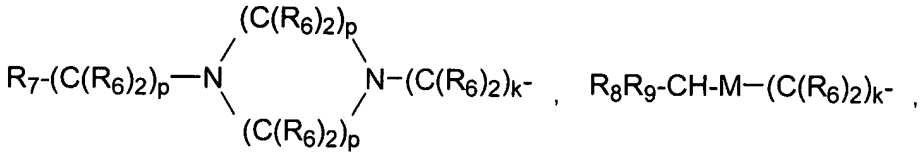
hereinabove in Step A with G'-C(L')$_3$, wherein G' is as defined hereinabove and L' is chloro, hydroxy, alkoxy, alkylthio, phenoxy, thiophenoxy or dimethylamine, or two L' groups can be taken together to form a substituent of =S, =NH, =O or =Se; by using acidic reaction conditions, basic reaction conditions, a strongly dehydrating solvent or 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline or by heating in an inert solvent, to provide the corresponding substituted 7-cyano-imidazo[4,5-g]quinolines of formula 32; and optionally converting the G' group of formula 32 to an R_2 group of formula 1 as defined in claim 1;

E) preparing a 7-cyano-imidazo[4,5-g]quinoline of formula 36



36

wherein Ar, X and n are as defined in claim 1, G' is as defined hereinabove and G" is selected from the group consisting of hydrogen, alkyl of 1-6 carbon atoms, cycloalkyl of 3-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, hydroxyalkyl of 2-6 carbon atoms, mercaptoalkyl of 2-6 carbon atoms, phenyl, benzyl,

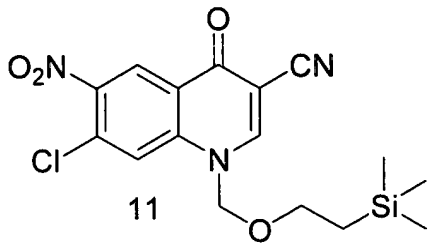


R_7-$(C(R_6)_2)_p$- , R_7-$(C(R_6)_2)_p$-M-$(C(R_6)_2)_p$- ,

Het-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_p$- and Ph-$(C(R_6)_2)_q$-W-$(C(R_6)_2)_p$- ,

wherein R_6, R_7, R_8, R_9, M, W, Het, Ph, p and q are as hereinabove defined, g = 2-6 and k = 2-4;

which comprises heating a compound of formula 11

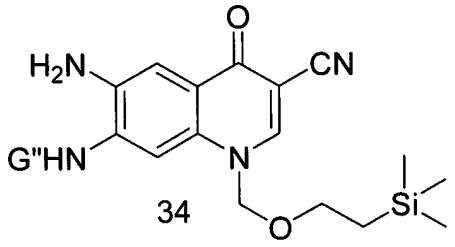


11

with an amine of formula 33

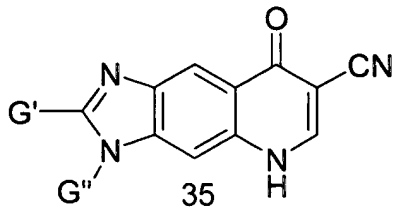
$$G''\text{-}NH_2$$

wherein G" is as defined hereinabove, in an inert solvent selected from the group consisting of acetonitrile and dimethyl sulfoxide (DMSO), and performing catalytic hydrogenation over palladium on carbon in tetrahydrofuran and ethanol to provide a compound of formula 34



34

reacting the compound of formula 34 with $G'\text{-}C(L')_3$, wherein G' and L' are as defined hereinabove, by using acidic reaction conditions, basic reaction conditions, a strongly dehydrating solvent or 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline or by heating in an inert solvent, to provide a compound of formula 35



35

wherein G' and G" are as defined hereinabove;

heating the compound of formula 35 with a chlorinating agent in the presence or absence of a solvent to provide the corresponding 8-chloroimidazo[4,5-g]quinoline-7-carbonitrile;

condensing the corresponding 8-chloroimidazo[4,5-g]quinoline-7-carbonitrile with a nucleophilic amine, aniline, mercaptan, thiophenol, phenol, or alcohol reagent of formula 5

$$HX-(CH_2)_n-Ar$$

5

wherein Ar, X and n are as defined hereinabove; optionally accelerating the condensation step by heating the reaction mixture together with one equivalent of pyridine hydrochloride or by using a base selected from the group consisting of trialkylamine, sodium hydride in an inert solvent, sodium alkoxide in an alcohol solvent and potassium alkoxide in an alcohol solvent, to give the 7-cyano-imidazo[4,5-g]quinolines of formula 36; and optionally converting the G' group of formula 36 or formula 35 to an R_2 group of formula 1 as defined in claim 1 and the G" group of formula 36 or formula 35 to an R_3 group of formula 1 as defined in claim 1;

F) resolving a mixture containing optically active isomers and recovering a racemate or an enantiomer when Ar, G' or G" as defined in claim 1 contains an asymmetric carbon atom;

G) separating, isolating and recovering a diastereomer when Ar, G' or G" as defined in claim 1 contains more than one asymmetric carbon atoms;

H) deprotecting and removing an amine or alcohol protecting group when Ar, G' or G" as defined in claim 1 contains a primary or secondary amino group or hydroxyl group requiring protection prior to a subsequent reaction step; or

I) acidifying a basic compound of formula 1 as claimed in claim 1 with a pharmaceutically acceptable acid to give a pharmaceutically acceptable salt.